FORM PTO-1390 (REV 5-93)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY DOCKET NO. 024118-00042
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		DATE: March 1, 2002
		U.S. APPLN. NO. (IF KNOWN, SEE 37 C.F.R. 1.5) 10/069125

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR00/02388	August 28, 2000	September 1, 1999

TITLE OF INVENTION: APPARATUS FOR ELECTRICAL STIMULATION OF THE LYMPHATIC SYSTEM AND USES THEREOF

APPLICANT(S) FOR DO/EO/US: Laurent PUJOL

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
(THE BASIC FILING FEE IS ATTACHED)

2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.

3. ☒ This express request to begin national examination procedures [35 U.S.C. 371(f)] at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. ☒ A proper demand for International Preliminary Amendment was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of the International Application as filed [35 U.S.C. 371(c)(2)]
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).

6. ☐ A translation of the International Application into English [35 U.S.C. 371(c)(2)].

7. ☒ Amendments to the claims of the International Application under PCT Article 19 [35 U.S.C. 371(c)(3)]
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.

8. ☐ A translation of the amendments to the claims under PCT Article 19 [35 U.S.C. 371(c)(3)].

9. ☐ An oath or declaration of the inventor(s) [35 U.S.C. 371(c)(4)].

10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 [35 U.S.C. 371(c)(5)].

Items 11 - 16 below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.

12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included.

13. ☐ A FIRST preliminary amendment.
☐ A SECOND or SUBSEQUENT preliminary amendment.

14. ☐ A substitute specification.

15. ☐ A change of power of attorney and/or address letter.

16. ☒ Other items or information: PCT Request; PCT/IPEA/416; PCT/IPEA/409; PCT/IPEA/408 (all in French) and PCT/ISA/210 (in French and English); Written Opinion; 46 sheets of Drawings (Figs. 1-45)

U.S. APPLN. NO. (IF KNOWN, SEE 37 C.F.R. 1.5) 10/069125	INTERNATIONAL APPLICATION NO. PCT/FR00/02388	ATTORNEY DOCKET NO. 024118-00042 DATE: March 1, 2002

17. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee [37 C.F.R. 1.492(a)(1)-(5)]: Search Report has been prepared by the EPO or JPO.....$890.00 International preliminary examination fee paid to USPTO (37 C.F.R. 1.482).....$710.00 No international preliminary examination fee paid to USPTO (37 C.F.R. 1.482) but international search fee paid to USPTO [37 C.F.R. 1.445(a)(2)].....$740.00 Neither international preliminary examination fee (37 C.F.R. 1.482) or international search fee [37 C.F.R. 1.445(a)(2)] paid to USPTO.....$1,040.00 International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4).....$ 100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date [37 C.F.R. 1.492(e)].	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	- 20 =		X $ 18.00	$	
Independent Claims	- 3 =		X $ 84.00	$	
Multiple dependent claim(s) (if applicable)			+ $280.00	$	
TOTAL OF ABOVE CALCULATIONS =				$ 890.00	
Reduction by one-half for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 C.F.R. 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$ 890.00	
Processing fee of $130.00 for furnishing the English translation later the ☐ 20 ☐ 30 months from the earliest claimed priority date [37 C.F.R. 1.492(f)]. +				$	
TOTAL NATIONAL FEE =				$ 890.00	
Fee for recording the enclosed assignment [37 C.F.R. 1.21(h)]. The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28, 3.31). $40.00 per property +				$	
TOTAL FEES ENCLOSED =				$ 890.00	
				Amount to be refunded	$
				Charged	$

a. ☒ A check in the amount of $890.00 to cover the above fees is enclosed.
b. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 01-2300.

NOTE: Where an appropriate time limit under 37 C.F.R. 1.494 or 1.495 has not been met, a petition to revive [37 C.F.R. 1.137(a) or (b)] must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
Arent Fox Kintner Plotkin & Kahn
1050 Connecticut Avenue, N.W.
Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000 Fax: (202) 638-4810
RBM/epb

Robert B. Murray
Reg. No. 22,980

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:
Laurent PUJOL

Appln. No.: 10/069,125

Filed: Concurrently herewith Attorney Dkt. No.: 024118-00042

For: APPARATUS FOR ELECTRICAL STIMULATION OF THE LYMPHATIC SYSTEM AND USES THEREOF

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

June 20, 2002

Sir:

Prior to calculation of the filing fees and initial examination of the application, please amend the above-identified application as follows:

IN THE CLAIMS:

Please amend claims 3, 4, 5, 6, 7, 8, 9, 10 and 11 as follows:

3. (Amended) The device as specified in claim 1, wherein such device is suitable for application of trains of pulses or "bursts" of 5/5 to 10/10 or to 15/15, preferably 10/10.

4. (Amended) The device as specified in claim 1, wherein each train of pulses exhibits reversal of polarity relative to the preceding train.

5. (Amended) The device as specified in claim 1, wherein the frequency of each pulse ranges from 0.1 to 3 Hertz, and preferably ranges from 0.7 to 2.5 Hertz, preferably near 11.5 or 2 Hertz.

6. (Amended) The device as specified in claim 1, wherein the pulses of electric current exhibit a working period ranging from 1 to 12, preferably 1 to 8, milliseconds, preferably 2 or 6 milliseconds.

7. (Amended) The device as specified in claim 1, wherein the pulses of electric current exhibit a rest period ranging from 300 to 900 milliseconds, preferably 400 to 700 milliseconds, preferably 500 or 650 milliseconds.

8. (Amended) The device as specified in claim 1, wherein such device is suitable for delivery of:

- a first type of current which is a "regulating or reeducating" current, useful primarily for treatment of pathological conditions of the lymphatic system and centered on a setting of around

2 milliseconds of work, 500 milliseconds of rest, 10/10 sequences > > 1.99 Hz

and/or

- a second type of "stimulating" or "turbo" current which provokes stimulation of the lymphatic system much stronger than the preceding one, useful primarily in

other applications of the device, physiological labor, and centered on a setting of around:

6 milliseconds of work, 650 milliseconds of rest, 10/10 sequences, > > 1.52 Hertz.

9. (Amended) The device as specified in claim 1, wherein the pulses of electric current exhibit preferably pulse trains of the 10/10 type.

10. (Amended) The device as specified in claim 1, wherein such device comprises at least two "contact" electrodes of the flat type, carbonated or non-carbonated, adhesive or non-adhesive, with or without hydrogel, positioned on or adhering to the epidermis

or

- "alligator" clips

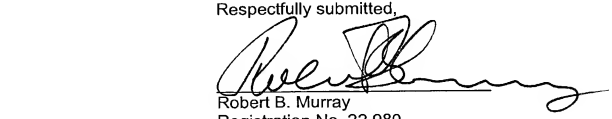
- needles implanted in the cutaneous tissue.

11. (Amended) The device as specified in claim 1, wherein such device comprises x couples of (+)(-) electrodes, such as two (+)(-) electrodes or four (+)(-) and (+)(-)electrodes covering two areas of treatment, etc. ...

REMARKS

Claims 1-11 are pending in this application. By this Amendment, claims 3, 4, 5, 6, 7, 8, 9, 10, 11 are amended to remove the multiple dependency thereof and to place this application into better condition for examination. No new matter is added.

Respectfully submitted,



Robert B. Murray
Registration No. 22,980

ARENT FOX KINTNER PLOTKIN & KAHN, PLLC
1050 Connecticut Avenue, N.W.,
Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000
Fax: (202) 638-4810
RBM/ars

Device for electric stimulation of the lymphatic system and applications of such device

This invention relates to the technical sector of electric stimulation of certain tissues.

Such techniques consist of sending electric stimuli to selected tissues, generally repetitive stimuli in the form of stimulating sequences capable of causing local stimulation of a given tissue and yielding a beneficial effect.

The invention applies more specifically to stimulation of the lymphatic system for the purpose of improving, stimulating, or restoring lymphatic drainage, on which overall balance of bodily fluids depends, including that of the circulatory and especially venous system.

General

The purpose of the lymphatic or lymphatico-venous system is to transport excess liquids, toxins, and wastes in the body, filter them, and remove them from the general circulation. This is the body's purification system; the ducts are not engorged when the lymph circulates properly. On the other hand, when for various reasons (overexertion, fatigue, obesity, age (loss of elasticity of tissues), pathology, exposure to pollution, genetic factors, aggravating factors such as tobacco, etc.), lymphatic circulation slows down, the interstitial tissues become filled with toxins and water. Well-known phenomena are then observed, ones such as

- Aging of tissues:

  bags under the eyes, wrinkles, flaccidity of the skin in general

- Pathology:

lymphostasis from

- aplasia or agenesia
- iatrogenic causes
- overflowing of the lymphatic system, in the event of hyperactivity due to a major venous problem.

- Cellulitis:

first stage = venolymphatic stage; the lymph is situated in the layer of fat which is hydrophobic (mobile stage);

second stage = infiltrate; the lymph is situated in septa around cells (establishment stage);

third stage = fibrosis tending toward sclerosis; gelatinization of the second stage involving, progressively, sclerosis of the tissue, states of tension presenting an "orange peel" appearance (stage characterized by low mobility, even sclerosis).

It is therefore important to be able to stimulate this system, in a specific and controlled manner, in order to achieve or improve "lymphatic drainage" in particular, that is, to stimulate the lymphatic ducts in a way well known to the expert by means of cycles of stimulation and relaxation. These operations mobilize the nerve cord by call to the lymph and "massage" to reabsorb the cord.

At the level of muscular tissues an overall distinction is made between white or smooth muscles and striated red muscles.

White or organic muscles are known to be muscles of organs, in particular of the small intestine, the stomach, and other known organs.

Veins as well are known to comprise very little white muscle.

It is also known that smooth or white muscles, which are present to a small extent or not present at all inside the veins (median part or tunica media or mediavenosa) have no striae.

Accordingly, the vein possesses no mobility of its own. It is the red muscles outside the vein which permit exertion of mechanical action on the vein (termed the "vis a latere/vein-pump effect").

On the other hand, the lymphatic collectors comprise white muscles (see Figure 44, the "lymphagion," and Figure 45). This is one of the major differences from the venous system (no lymphatic varices) and it is this which renders this system dynamizable by mechanical and electric means.

- The primary collectors, because of their system of stays connected to the tissue (see Figure 45), will themselves be dynamized by stretching or depression of the skin;

- The lymphatic ganglia are not provided with muscles; hence stimulation of them is much more difficult.

Presented in diagrammatic form in Figure 45 attached, which consists of Figures 45A and 45B, are the "precollectors" at rest (Figure 45A) and at work (Figure 45B). It is to be seen that the walls 120 of the precollectors are connected to the conjunctive tissue or "interstitium" (not shown in detail) by "stays" 140.

Because these stays are fixed in the tissues, any depression, any increase in volume, any stretching, will stretch these stays and consequently increase the drainage efficiency of these stays.

Stretching of tissue may be effected by

- movement of a member,

- increase in volume of a member when edema is present,

- adaptation to stress (movement + increase in perfusion and in liquid in circulation).

In the rest stage the walls 120 are not tightly jointed and the "aperture" 130 of the precollector is reduced. In the work stage, in contrast, the walls remain loosely jointed, but stretching of the stays 140 causes increase in the "aperture" 130.

Hence the technical problem of lymphatic system stimulation is radically different from that relating to the venous system.

The waste elimination system, including the lymphatic system, is of the following composition, and its operation is outlined in what follows.

On the basis of an arterial system, which leads into the tissues of food substances, oxygen, and liquids, there is a system for elimination of wastes and renewal of liquids.

• The evacuation system is dual in nature:

- The venous system : system for rapid regeneration of liquids, minor waste substances (CO_2, etc) with the osmotic pressure and onchotic pressure in tissue maintained in accordance with Starling's Law 1 and 2).

- The lymphatic system: much slower system of management of liquids and elimination of major wastes; it also participates in immunology by transporting the lymphocytes which form part of the immunity system.

• Lymph is the tissue absorption liquid. 80% of this lymph is situated between the epidermis and the surface muscle aponeurosis.

• The lymphatic network represents 500 m^2 of exchange and evacuation area (system cut flat).

The lymphatic system is the true manager of hydration and also the "scavenger" of these tissues; it also participates in immunology, as explained above.

In its tissues this system is made up of a majority of muscles, in contrast to the venous system.

The lymphatic lattice proceeding from vascular fissures is made up of a terminal dendrite of primary collectors with direct or indirect openings made up of loosely joined cells linked to the tissues by stays; any increase in volume, any shifting of the tissues, stretches these stays, opens these tubules, and the lymph is drawn into the system as a result of increase in pressure.

• The following stage enables the lymph to circulate in precollectors, the lymphatic tubule begins to become endothelialized, and ultimately the lymph arrives at the level of the lymphatic collectors.

The lymphatic collector is a separate organized vessel as shown in Figure 44. This collector is provided with valvulae which send the lymphatic current in a mandatory direction. Between these valvulae a peristaltic wave, a muscular contraction of each lymphangion, passes with a slow automatic rhythm (with the possibility of sympathetic and parasympathetic variations) in the distoproximal direction through the tubular tissue made up of white muscles (subject to the sympathetic and parasympathetic neurovegetative system).

- These collectors arrive at the ganglia (afferent vessels).

- These ganglia are not muscles; what is involved is a veritable "waste recycling plant," and the ganglia operate by absorbing the lymph in the ganglionic tissue.

Two lymph cleaning systems are :

-- phagocyte system = phagocytes "digest" the inert elements (having no genetic material) to produce simple molecules,

-- immunity system = recognition of a different genetic material (bacteria, viruses, metastases, ...); the macrophages and lymphocytes "kill" these different cells and disorganize the DNA in order to sever the amino connections and return to circulation simple non-combined acids, ones which are inoffensive and may even be reused by the body to produce new DNA chains in its own image.

- A system of adaptation to stress consists of twofold circulation, slow and fast:

— slow = see above

— fast = one part of the lymph is treated not on a first ganglion but on the following ones (the one treated by slow circulation at the outset is then shifted to fast circulation). On arrival at the heart the lymph is "clean"; the vessels which distribute ganglia are called afferent vessels.

The lymphatic or lymphaticovenous system has the function of carrying liquids and excess toxins in the body, filtering them, and discharging them into lymphatic and blood circulation. It is the body's cleansing system; when lymph is circulating properly, the ducts are not clogged. On the other hand, when for various reasons, such as overwork, fatigue, obesity, age (loss of elasticity of tissues), pathological conditions, exposure to pollution, genetic factors, aggravating factors

such as tobacco, etc., lymphatic circulation slows down, interstitial tissues begin to be filled with toxins. Well known phenomena such as formation of bags under the eyes, facial wrinkles, etc., as well as phlebitis, swelling of members, etc., begin to be observed.

Consequently, this lymphatic system is manager of the quality of tissues and of effective immunological defense of the body, the object of the therapeutic aims of the invention.

The following patents in this field are known:

FR 2 541 119 (Klotz), whose object it is to stimulate the smooth muscles by progressive impulses, or USP 4 177 819, or FR 2 433 950, or FR 2 528 709, or USP 4 068 669, or USP 3 645 267, or USP 3 050 695, or USP 3 0077 884, or, lastly, USP 4 167 189, which measures impedance and applies a sine wave signal, and EP 0 057, EP 0 148 312, EP 0425 673, and FR 2 704 151 whose object it is to measure impedance.

In the opinion of the Applicant, the proximate prior art is represented by the following patents:

FR 2 541 119, FR 2 704 151, USP 4 167 189, EP 0 425 673. These technologies are presented as stimulating the white (smooth) muscles of the venous media and acting at all times on the venous system.

Also of the state of the art is patent WO 91 07207, which describes application of a pulsed current for the purpose of lymphatic drainage.

It has now been found that the lymphatic or lymphatico-venous system in man or animal, especially the horse, may be stimulated by means of specific electric stimuli which are to be described in what follows.

The invention relates to a new process and a new device for stimulation of the lymphatic system in man or in animals, the horse in particular, characterized in that such process consists in, or

permits, application of at least two electrodes to the skin and causes sequences of electric stimuli to pass into the human or animal body involved (hereinafter referred to jointly and severally as "the body"), each stimulus or pulse being characterized in that

- the period of excitation is shorter than the period of rest or relaxation;

- the period of excitation ranges from 2 to 8 milliseconds;

- the period of rest or relaxation ranges from 400 to 850 milliseconds.

In one particular application, the intensity of the electric current applied is lower than or equal to 1 mA (milliampere), and preferably of the order of 6 to 300 microamperes (mA) or more, depending on the number of electrodes which, along with the patient's "feeling" (physical response), represent the only restrictions imposed in this context.

In a preferred embodiment pulse trains or "bursts" of 5/5 to 10/10 or 15/15, preferably 10/10, are to be applied.

Each train or sequence of pulses exhibits reversal of polarity relative to the preceding sequence. Consequently, the mean value of the current is zero; this prevents any polarization of material in the tissue treated.

In a specific embodiment, the frequency of each pulse is to range from 0.1 to 3 Hz, and preferably from 0.7 to 2.5 Hz, preferably in the vicinity of 1.5 or 2 Hz.
Other characteristics and advantages of the invention will be better understood by reading of the following description and by referring to the tests and to the attached drawing, in which

- Figures 1 to 43 present the curves of EMG activity obtained with the device claimed for the invention and with devices of the prior art, as specified in the TESTS presented below.

- Figure 44 represents a "lymphangion."

- Figure 45, which consists of Figures 45A and 45B, presents the structure of the tissues around the lymphatic system.

TESTS

General mode of operation

Three anatomical parts were taken from swine recently sacrificed (5 minutes earlier): the heart, certain blood vessels, the lungs, and the small intestine.

Dissection was performed and the following anatomical elements were selected:

- vena cava 10 cm/40 g

- thoracic canal (canalis lymphaticus major) and small intestine making up a total of 150 g

- red skeletal muscles 150 g

Tests were also conducted with healthy humans (referred to as "SUBJECT" in what follows).

The tests were conducted with a device of the EMG type with biofeedback (visual graphic inspection of the contraction) of the YSY EST™ type made by the YSY MEDICAL™ company capable of performing EMG measurements (activity - electromyogram) and comprising a system of filters designed to register only the activity of the tissues (especially contractions) and not interfering signals.

The pulses were applied, as appropriate, either with needles planted in the test tissue (referred to as "ACU" in what follows) or by alligator clips clamping the test tissues ("CROCO").

This testing procedure has been deemed to be suitable for proper simulation of "external non-invasive" stimulation procedures by contact electrodes, which are the ones employed in practice, except in precisely identified particular cases.

The purpose of the tests was to compare the effects of different devices at different settings in order to determine the forms and characteristics of current suitable for treating or stimulating the lymphatic system in accordance with the objectives cited in the foregoing.

Activity was calculated by means of a formula determining the mean of positive and negative pulses established by taking account of, and relative to, the "path acquisition" which is displayed in the window to the left of the curves, which will be understood by the expert.

TEST No. 1

Comparative test of Datavein™ and the FDLP device claimed for the invention.

The device is set in accordance with the operating instructions for the Datavein™, that is, at 1.75 Hz (frequency of each pulse), work time of 4 millisec, intensity of 6 μA, and a rest period of 567 millisec, with 8/8 electric pulses.

Figure 1 presents the EMG results obtained with the Datavein™ device, and Figure 2 the results obtained with the FDLP device at the same settings.

The positioning of cursors permits calculation of representative and reproducible averages.

It is to be seen that average EMG activity is 2900 for the Datavein™ and 4143 for the FDLP, that is, activity approximately twice as high for the second device, at the same settings.

The widely differing shape of the curves is also to be noted.

TEST No. 2

The Datavein™ and FDLP devices were compared.

The FDLP was set to the values recommended for the Datavein™ (identified by the reference "FDLP DATA").

The test was conducted with lymphatic tissue or of the lymphatic type of swine (lymphatic tissue and small intestine (referred to as "LYMP") and by means of alligator clips (referred to as "CROCO").

The EMG activity measured with the Datavein™ is 1014 (Figure 4b) and 10971 (Figure 3) with the FDLP, which is seen to yield an effect ten times greater.

Note is also to be made of the different form of the pulses, and, with the Datavein™, regular pulses are observed, while pulses alternating in groups of eight with inversion of polarity are observed with the FDLP, but not with the Datavein™.

TEST No. 3

The Datavein™ and FDLP devices were compared.

The test was conducted with a human being ("SUBJECT") by means of the Datavein™ with two tests (Figures 4 and 5) and the FDLP with the Datavein™ settings (Figure 6) and thus more than with the Datavein™ (Figure 7).

The devices were set to 30 μA.

It is to be seen that the activity measured with the FDLP with the Datavein™ setting is 10604 (Figure 6), while that measured with the Datavein™ is 1413 (Figure 7), 1554 (Figure 8) 5086 (Figure 4), 4844 (Figure 5).

Hence the FDLP is 2 to 7 times more powerful than the Datavein™ in this test.

TEST No. 4

An effort was made in this test to compare the physical "feeling" of a human subject when treated with the Datavein™ or with the FDLP.

It was found that, in order to find the feeling of the FDLP set to only 30 μA, it was necessary to increase the intensity delivered by the Datavein™ to 150 μA.

This is confirmed by Figures 9 and 10 (Datavein™) set to 154 μA; the average EMG is 10340 or 10616.

It is useful to make a comparison with Figure 6 (FDLP set to the parameters recommended for the Datavein™), which delivered a mean activity of 10604 at 30 μA, while the Datavein™ produced only 1413 at the same intensity.

TEST No. 5

The overall superiority of the FDLP having been demonstrated above in various configurations, this test was undertaken to investigate the best current characteristics for the FDLP.

Figure 11 illustrates the activity curve in a subject of the FDLP set to 6 millisec work time, 500 millisec rest time, 10/10 sequences or "bursts," and 6 μA intensity.

Figure 12 shows the same curve, except that the sequences are 5/5 rather than 10/10.

A mean activity of 5796 is observed for the 10/10 curve, in contrast to 5343 for the 5/5 curve.

The two activities are thus more or less equivalent, but the setting at 10/10 produces a more comfortable "feeling" than at 5/5.

An attempt has been made to explain this phenomenon and, without wanting to be tied to any theory, the applicant believes that the 10/10 setting is better suited to the slow rhythm of the natural oscillations of the lymphatic system. In order to stimulate a ganglion manually, the expert will perform 6 to 8 oscillations per minute, which corresponds to a frequency of the order of 0.1 Hz. A lymphatic collector performs 10 12 movements per minute, at a frequency of the order of 0.2 Hz.

The FDLP 10/10 setting, with 6 millisec of work and 650 millisec of rest, at 6 μA, yields a frequency of the order of 1.52 Hz.

The FDLP 10/10 setting, with 2 millisec of work and 500 millisec of rest, at 6 μA, yields a frequency of the order of 1.99 Hz.

It appears that the combination of these two frequencies and pulse trains harmonize with the natural slow rhythm of the lymphatic system.

The setting recommended for the Datavein™ is 1.75 Hz.

At the same setting the Datavein™ yields only values of 2900 or 1413 (Figures 1 at 6 μA and 7 at 30 μA), and accordingly in this test reveals an efficiency even less than one-half that of the FDLP.

TEST No. 6

Comparison was made again in this test of two different FDLP settings, one (Figure 13) with a human subjects, with 2 millisec of work, 650 millisec of rest and 10/10 sequences, at 6 μA, and the other (Figure 14) with a human subject with 2 millisec of work, 500 millisec of rest and 5/5 sequences.

The mean efficiency obtained in Figure 14 is 677, as against 1911 in Figure 13.

Hence, it appears to be more efficient to provide a long rest time for the same work time.

It also appears to be more interesting to provide sequences of 10/10, this confirming a previous test.

TEST No. 7

The FDLP was tested on a human subject with a setting of 6 millisec of work time, 650 millisec of rest time, and sequences of 10/10, at 30 μA/

An EMG activity of 8435 was obtained (Figure 15).

INTERIM FINDING

The foregoing tests on the one hand reveal efficiency 2 to 10 times greater for the FDLP than for the Datavein™, and, on the other hand, indicate the possibility of setting the FDLP device for generation of current of two types:

- a first type of current is a "regulator" or "reeducator" current, useful primarily for treatment of pathological conditions of the lymphatic system, one which is centered on a setting of approximately:

2 millisec of work 500 millisec of rest 10/10 sequences > > 1.99 Hz

- a second type of "stimulator" or "turbo" current, causing stimulation of the lymphatic system much stronger than the preceding one, useful primarily in other applications of the FDLP, physiological work, and centered around a setting of approximately

6 millisec work 650 millisec rest 10/10 sequences > > 1.52 Hz.

TEST No. 8

Tests were conducted with venous tissue, either with implanted needles or with alligator clips.

In order to obtain the curves shown in Figures 16, 17, and 18 use was made of a FDLP with Datavein™ settings ("FDLP DATA") with alligator clips ("CROCO) and with venous tissue ("VEINE"). Activities of 11900, 12007, and 12122 were obtained.

In order to make a comparison with the Datavein™ a test was also conducted with the Datavein™ at the settings recommended by the manufacturer, on venous tissue and with alligator clips (Figure 20). A value of only 9187 was obtained.

Consequently, the FDLP clearly performs better than the Datavein™ even with venous tissue.

The FDLP with Datavein™ settings was also tested on venous tissue but with needles ("ACU") implanted (Figure 19). A value of 10889 was obtained, that is, a value lower than those obtained with the alligator clips. This appears to invalidate the theory of the Klotz patent to the

effect that the veins are made up of white muscles. In fact, in a case such as this the ACU effect should have been greater than the CROCO effect.

TEST No. 9

Tests were conducted:

- with red muscle using FDLP with Datavein™ settings, with needles (Figure 21). Activity (mean): 5344.

- with red muscle using FDLP with Datavein™ settings, with alligator clips (Figure 22). Activity: 1856.

- with red muscle using Datavein™, with alligator clips (Figure 23). Activity: 1172. Hence the result obtained with Datavein™ is not as good as that obtained with FDLP.

TEST No. 10

"Regulator" current tests were conducted with the FDLP:

- with red muscle, using the FDLP set for 2 millisec work, 500 millisec rest, needles, and 10/10 trains (Figure 24): activity: 2730.

- with red muscle, using the FDLP set for 2 millisec work, 500 millisec rest, needles, and 5/5 sequences (Figure 25): activity: 3215.

It is clearly to be seen from the curves that the 5/5 setting is superior to the 10/10 setting for the red muscle, while the opposite finding applies to the lymphatic tissue (performance with 10/10 setting higher with lymphatic tissue).

TEST No. 11

Square wave signal tests were conducted.

Use was made of the MICROSTIM™ device of the Physio-INSEP™ company, the manufacturer of which asserts that the device operates as a "vein pump" or by the effect of pumping on the striated red skeletal system peripheral to the venous system (by contraction-relaxation), at an initial setting of 1.25 Hz.

The following curves were obtained:

Croco with lymphatic tissue (Figure 26); result mediocre

Needles with lymphatic tissue (Figure 27); result somewhat better

Croco with red muscle (Figure 28); good result (3554)

Needles with red muscle (Figure 29); good result (2323)

Croco with venous tissue (Figure 30); 9567

Needles with venous tissue (Figure 31); 1584

The good results reflected in Figures 28 to 31 were predictable, because the device is designed for "vein pump" operation by stimulating the perivascular skeletal striated muscles.

The MICROSTIM™ device was then used at a second setting of 1.50 Hz.

The following curves were obtained:

Croco on lymphatic tissue (Figure 32)	mediocre results 1345
Needles in lymphatic tissue (Figure 33)	7551 needle problem
Croco on red muscle (Figure 34)	good result 3779
Needles in red muscle (Figure 35)	good but inferior result
Croco on venous tissue (Figure 36)	10002 very good result
Needles in venous tissue (Figure 37)	10901 very good result

It was inferred that application of square wave signals is better suited for treatment of the venous system, because the stimulation affects the striated perivascular muscles but not at all, or very slightly, the mediavenous, which is almost absent from the venous systems as a whole.

The MICROSTIM™ device was then used at a third setting of 1.75 Hz, which is the setting recommended for the Datavein™ by its manufacturer.

The following curves were obtained:

Croco on lymphatic tissue (Figure 38)	very mediocre result 909
Needles in lymphatic tissue (Figure 39)	average result 1729
Croco on red muscle (Figure 40)	average result 1668
Needles in red muscle (Figure 41)	good result 7006

Croco on venous tissue (Figure 42)	10 339 very high activity
Needles in venous tissue (Figure 43)	10 893 very high activity

Although the low quality of perivascular red muscles could distort certain results of this test, these multiple tests do show that the device exerts a very clearcut effect on the vein and a red muscle (in the manner of a vein pump, with a very pronounced contraction effect), more so than on the lymphatic system, where the effect is virtually zero.

This indicates that the square wave signals exert no significant effect on the lymphatic system.

Such tests also have the merit of validating all the other tests indicated above which have been performed, because they make it possible to duplicate the results announced by the manufacturer. It may be inferred that the tests performed with the FDLP and with the Datavein™ are significant.

The invention thus relates to a device for stimulation and treatment of the lymphatic system (this term applying for the sake of simplicity to all the effects and all the applications referred to in the foregoing), a device which comprises an electric pulse generator and at least two electrodes which are positioned on the epidermis of the subject to be treated, characterized in that such electric current pulses are not in the form of square wave signals.

In one specific embodiment the device is characterized in that the electric current pulses have a work time ranging from 1 to 12, preferably 1 to 8, preferably 2 or 6, millisec.

In one particular embodiment the device is characterized in that the electric current pulses have a rest time ranging from 300 to 900 millisec, preferably from 400 to 700 millisec, preferably 500 or 650 millisec.

In one specific embodiment the device is characterized in that the electric current pulses exhibit a current intensity of 6 to 300 μA, preferably 6 to 50 or 100 or 150 μA, or more, depending on the sensitivity ("feeling") of the patient and on the number of electrodes (2, 4, 6, etc.; see below), as the expert will readily understand.

In another specific embodiment the device is characterized in that the electric current pulses exhibit a frequency of around 0.1 to 3 Hz, preferably around 1.99 Hz or around 1.52 Hz.

In another specific embodiment the device is characterized in that the electric current pulses exhibit pulse trains.

In another specific embodiment the device is characterized in that the electric current pulses preferably exhibit pulse trains of the 10/10 type.

In another specific embodiment the device is characterized in that the electric current pulses exhibit pulse trains with reversal of polarity between each sequence.

In one specific embodiment the device is characterized in that the electric current pulses are set at:

Work time	2 millisec
Rest time	500 millisec
Pulse trains	10/10
Frequency	1.99 Hz,

this producing a "regulating" or "reeducating" current for treatment of pathological or deficient lymphatic systems.

In one specific embodiment the device is characterized in that the electric current pulses are set at:

Work time	6 millisec
Rest time	650 millisec
Pulse trains	10/10
Frequency	1.52 Hz,

this producing a "stimulating" or "turbo" current applying a very strong effect of stimulating the lymphatic system. Consequently, this current will be more suitable for accelerating or activating the non-pathological lymphatic system.

In another specific embodiment the device is characterized in that the electric current pulses are applied by:

- epidermal "contact" electrodes, of the flat type, carbonated or not, adhesive or not, with or without hydrogen, positioned on or adhering to the epidermis

and, optionally, in certain cases identified precisely by the practitioner

- clips of the "alligator" type,

- needles implanted in the cutaneous tissue.

In another particular embodiment the device is characterized in that the electric current pulses are applied by at least two electrodes.

In another particular embodiment the device is characterized in that the electric current pulses are applied by x electrode couples such as two (+)(-) electrodes or four (+)(-) electrodes covering two treatment areas, etc.

The applications of the invention, device and process, are represented by non-restrictive examples such as the following:

in the area of esthetics:

- treatment of cellulitis

- facial care (edema, undernourished skin)

- scars

in the case of pathological conditions:

- lymphostasis as described above

- venous disorders
- excessively strained muscles/muscular regeneration
- scars
- inflammation, tendinitis
- lymphology/phlebology/traumatology/athletic traumatology/rheumatology/dermatology/surgery/geriatrics/ gastroenterology/gynecology/obstetrics/treatment of burns

in immunology

and, in the horse or other animals such as the dog in particular:

- all pathological circulatory conditions, laminitis and other pathological excess stress conditions (muscular regeneration, scars, inflammation, tendinitis, tendinopathies including tendinitis, pathological muscular or osteo-articular conditions)

- pathological condition of working muscles, in the horse,

and other analogous human or veterinary applications which will be obvious to and within the sphere of knowledge of the expert.

Mark up Claims

CLAIMS

1 A device for stimulation of the lymphatic system in the human or animal, the horse in particular, *characterized in that* such device comprises a generator of electric pulses and at least two electrodes which are positioned on the epidermis of the subject to be treated so as to cause electric stimulation trains to pass into the human or animal body involved (hereinafter referred to jointly and separately as the "body"), each stimulation or pulse being characterized in that

- square wave signals are not involved

- the excitation period is shorter than the rest or relaxation period;

- the excitation period ranges from 2 to 8 milliseconds;

- the rest or relaxation period ranges from 400 to 850 milliseconds.

2 The device as specified in claim 1, *wherein* the intensity of the electric current applied is lower than or equal to 1 mA (one milliampere), and is preferably of the order of 6 to 300 μA (one microampere), preferably 6 to 50 or 100 or 150 or more, depending on the number of electrodes.

3 The device as specified in claim 1 [or 2], *wherein* such device is suitable for application of trains of pulses or "bursts" of 5/5 to 10/10 or to 15/15, preferably 10/10.

4 The device as specified in [any one of claims] 1 [to 3], *wherein* each train of pulses exhibits reversal of polarity relative to the preceding train.

5 The device as specified in any one of claims 1 to 4, *wherein* the frequency of each pulse ranges from 0.1 to 3 Hertz, and preferably ranges from 0.7 to 2.5 Hertz, preferably near 11.5 or 2 Hertz.

6 The device as specified in any one of claims 1 to 5, *wherein* the pulses of electric current exhibit a working period ranging from 1 to 12, preferably 1 to 8, milliseconds, preferably 2 or 6 milliseconds.

7 The device as specified in any one of claims 1 to 6, *wherein* the pulses of electric current exhibit a rest period ranging from 300 to 900 milliseconds, preferably 400 to 700 milliseconds, preferably 500 or 650 milliseconds.

8 The device as specified in any of claims 1 to 7, *wherein* such device is suitable for delivery of:

- a first type of current which is a "regulating or reeducating " current, useful primarily for treatment of pathological conditions of the lymphatic system and centered on a setting of around

2 milliseconds of work, 500 milliseconds of rest, 10/10 sequences > > 1.99 Hz

and/or

- a second type of "stimulating" or "turbo" current which provokes
stimulation of the lymphatic system much stronger than the preceding one, useful primarily in other applications of the device, physiological labor, and centered on a setting of around:

6 milliseconds of work, 650 milliseconds of rest, 10/10 sequences, > > 1.52 Hertz.

9 The device as specified in any one of claims 1 to 8, *wherein* the pulses of electric current exhibit preferably pulse trains of the 10/10 type.

10 The device as specified in any one of claims 1 to 9, *wherein* such device comprises at least two "contact" electrodes of the flat type, carbonated or non-carbonated, adhesive or non-adhesive, with or without hydrogel, positioned on or adhering to the epidermis

or

- "alligator" clips

- needles implanted in the cutaneous tissue.

11 The device as specified in any of one claims 1 to 11, *wherein* such device comprises x couples of (+)(-) electrodes, such as two (+)(-) electrodes or four (+)(-) and (+)(-) electrodes covering two areas of treatment, etc. ...

(12) DEMANDE INTERNATIONALE PUBLIÉE EN VERTU DU TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS (PCT)

(19) Organisation Mondiale de la Propriété Intellectuelle
Bureau international

(43) Date de la publication internationale
8 mars 2001 (08.03.2001)

PCT

(10) Numéro de publication internationale
WO 01/15772 A1

(51) Classification internationale des brevets[7]: A61N 1/32

(21) Numéro de la demande internationale:
PCT/FR00/02388

(22) Date de dépôt international: 28 août 2000 (28.08.2000)

(25) Langue de dépôt: français

(26) Langue de publication: français

(30) Données relatives à la priorité:
99/11043 1 septembre 1999 (01.09.1999) FR

(71) Déposant *(pour tous les États désignés sauf US)*: ALOHA S.A. [FR/FR]; 9, chaussée Jules César, Boîte Postale 513 Osny, F-95528 Cergy Pontoise Cedex (FR).

(72) Inventeur; et

(75) Inventeur/Déposant *(pour US seulement)*: PUJOL, Laurent [FR/FR]; Aloha, 9, chaussée Jules César, Boîte Postale 513 Osny, F-95528 Cergy Pontoise Cedex (FR).

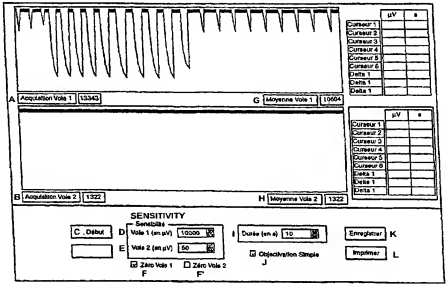
(74) Mandataire: RICHEBOURG, Michel; Cabinet Michel Richebourg, 69, rue Saint Simon, Le Clos du Golf, F-42000 Saint Etienne (FR).

(81) États désignés *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

[Suite sur la page suivante]

(54) Title: APPARATUS FOR ELECTRICAL STIMULATION OF THE LYMPHATIC SYSTEM AND USES THEREOF

(54) Titre: APPAREIL DE STIMULATION ELECTRIQUE DU SYSTEME LYMPHATIQUE, ET SES APPLICATIONS



A ...PATH 1 ACQUISITION
B ...PATH 2 ACQUISITION
C ...START
D ...PATH 1 (in V)
E ...PATH 2 (in V)
F ...ZERO PATH 1
F'...ZERO PATH 2
G ...MEAN PATH 1
H ...MEAN PATH 2
I ...DURATION IN SECONDS
J ...SIMPLE OBJECTIVATION
K ...RECORD
L ...PRINT
CURSEUR = CURSOR

Fiche Patient : FDLP DATA SUJET 2.
Date de la Séance : Mercredi 2/6/1999.
2 Voies de Muscle.

PATIENT FILE: FDLP DATA SUBJECT 2
DATA IF SESSUIB WEDBESDAY 2/6/1999.
TWO MUSCLE PATHS

(57) Abstract: The invention concerns an apparatus for stimulating the lymphatic system by electrical stimulation. Said apparatus comprises a system of electrodes arranged on the skin at sites known to the practitioner, and sends a series of electrical stimuli for accurately stimulating the elements of the lymphatic system. The invention is particularly useful for lymph-drainage in humans and animals, in particular horses and dogs.

(57) Abrégé: L'invention concerne un appareil pour la stimulation du système lymphatique par des excitations électriques. L'appareil comporte un système d'électrodes qui sont disposées sur la peau aux endroits appropriés connus du praticien, et envoie un train de stimuli électriques adaptés pour stimuler précisément les éléments du système lymphatique. Applications entre autres au drainage lymphatique chez l'homme et l'animal, notamment le cheval et le chien.

WO 01/15772 A1

PATENT APPLICATION

Title: **A device for electric stimulation of the lymphatic system and applications of such device**

Inventor: **Laurent Pujol**

Applicant: **Aloha S. A.**

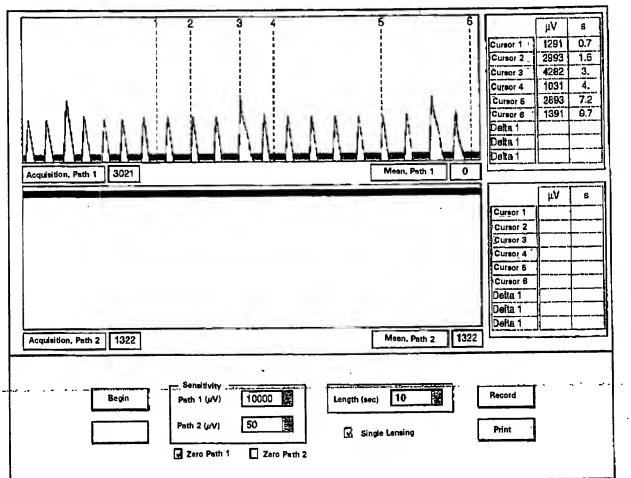
Abstract

The invention relates to a device for stimulation of the lymphatic system through electric excitation.

The device comprises a system positioned on the skin at suitable places known to the expert and sends a train of electric stimuli suitable for stimulating specifically the elements of the lymphatic system.

Applications include lymphatic drainage in man and animals, especially the horse and the dog.

Figure 6



Patient Chart: SUBJECT DATA

Date of Session: Wednesday, June 2, 1999

2 Muscle Paths

YSY EST - 1998 YSY MEDICAL -

FIG. 1

Acquisition, Path 1
3508
Mean, Path 1
4149
Acquisition, Path 2
1322
Mean, Path 2
1822
Cursor 1
Cursor 2
Cursor 3
Cursor 4
Cursor 5
Cursor 6
Delta 1
Delta 1
Delta 1
µV
s
1349
0.7
3498
1.4
465
2.4
8466
3.6
9327
5.3
1307
8.
Begin
Sensitivity
Path 1 (µV)
Path 2 (µV)
10000
50
Zero Path 1
Zero Path 2
Length (sec)
10
Single Leveling
Record
Print
Patient Chart: FDLP SUBJECT DATA
Date of Session: Wednesday, June 2, 1999
2 Muscle Paths

FIG. 2

#4

Docket No. 024118-00042 ARENT FOX KINTNER PLOTKIN & KAHN, PLLC

Declaration For U.S. Patent Application

As a below named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below my name.
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention **entitled**
(Insert Title) APPARATUS FOR ELECTRICAL STIMULATION OF THE LYMPHATIC SYSTEM AND USES THEREOF

the specification of which is attached hereto unless the following box is checked:

☒ was filed on August 28, 2000 As PCT International Application
Number PCT/FR00/02388 and was amended on _____
and/or was filed on March 1, 2002 As U.S. Patent Application
Number _____ and was amended on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claim(s), as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. §1.56.
I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate or PCT International Application having a filing date before that of the application(s) for which priority is claimed:

				Priority Claimed
(List prior foreign applications)	99/11043 (Number)	France (Country)	1 September 1999 (Day/Month/Year Filed)	☒ Yes ☐ No
	(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes ☐ No
	(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes ☐ No

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

(Application Number) (Filing Date)
(Application Number) (Filing Date)

☐ See attached list for additional prior foreign or provisional applications.

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) or §365(c) of any PCT International application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior application(s) (U.S. or PCT) in the manner provided by the first paragraph of 35, U.S.C. §112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

(List prior U.S. Applications or PCT International applications designating the U S.)	(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
	(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

17

And I hereby appoint the firm of Arent Fox, Customer Number 004372 including as principal attorneys: Robert B. Murray, Reg. No. 22,980; Charles M. Marmelstein, Reg. No. 25,895; George E. Oram, Jr., Reg No. 27,931; Douglas H. Goldhush, Reg. No. 33,125; Richard J. Berman, Reg. No. 39,107; Murat Ozgu, Reg. No. 44,275; Robert K. Carpenter, Reg. No. 34,794; Rustan Hill, Reg. No. 37,351; Kevin Turner, Reg. No. 43,437; Rhonda L. Barton, Reg. No. 47,271; Hans J. Crosby, Reg. No. 44,634, Brian A. Tollefson, Reg. No. 46,338; David D. Dzara, Reg. No. 47,543, Lynne D. Anderson, Reg. No. 46,412; Dinnatia J. Doster, Reg. No. 45,268, Michael A. Steinberg, Reg. No. 43,160 and Lynn A. Bristol, Reg. No. 48,898.

Please direct all communications to the following address:

Customer No. 004372
ARENT FOX KINTNER PLOTKIN & KAHN, PLLC
1050 Connecticut Avenue, N.W., Suite 400
Washington, D.C. 20036-5339
Telephone No. (202) 857-6000; Facsimile No. (202) 638-4810

The undersigned hereby authorizes the U.S. attorneys named herein to accept and follow instructions from the undersigned's assignee, if any, and/or, if the undersigned is not a resident of the United States, the undersigned's domestic attorney, patent attorney or patent agent, as to any action to be take in the Patent and Trademark Office regarding this application without direct communication between the U.S. attorneys and the undersigned. In the event of a change in the person(s) from whom instructions may be taken, the U.S. attorneys named herein will be so notified by the undersigned

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1-00

Full name of sole or first inventor Laurent PUJOL

Inventor's signature _____ 25 02 2002
Date

Residence Cergy Pontoise Cedex France
Citizenship France
Post Office Address 9, Chaussee Jules Cesar, Boite Postale 513 Osny
F-95528 Cergy Pontoise Cedex France

Full name of second inventor _____

Inventor's signature _____ Date

Residence _____
Citizenship _____
Post Office Address _____

Full name of third inventor _____

Inventor's signature _____ Date

Residence _____
Citizenship _____
Post Office Address _____

Full name of forth inventor _____

Inventor's signature _____ Date

Residence _____
Citizenship _____
Post Office Address _____

Full name of fifth inventor _____

Inventor's signature _____ Date

Residence _____
Citizenship _____
Post Office Address _____

Full name of sixth inventor _____

Inventor's signature _____ Date

Residence _____
Citizenship _____
Post Office Address _____